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Inventor: Townes et al.  
Application No. 10/659,675  
Docket No. 21085.0053U5  
Sheet: 1 of 16  
REPLACEMENT DRAWINGS

## MATING SCHEME FOR PRODUCTION OF HbA REPLACEMENT MICE

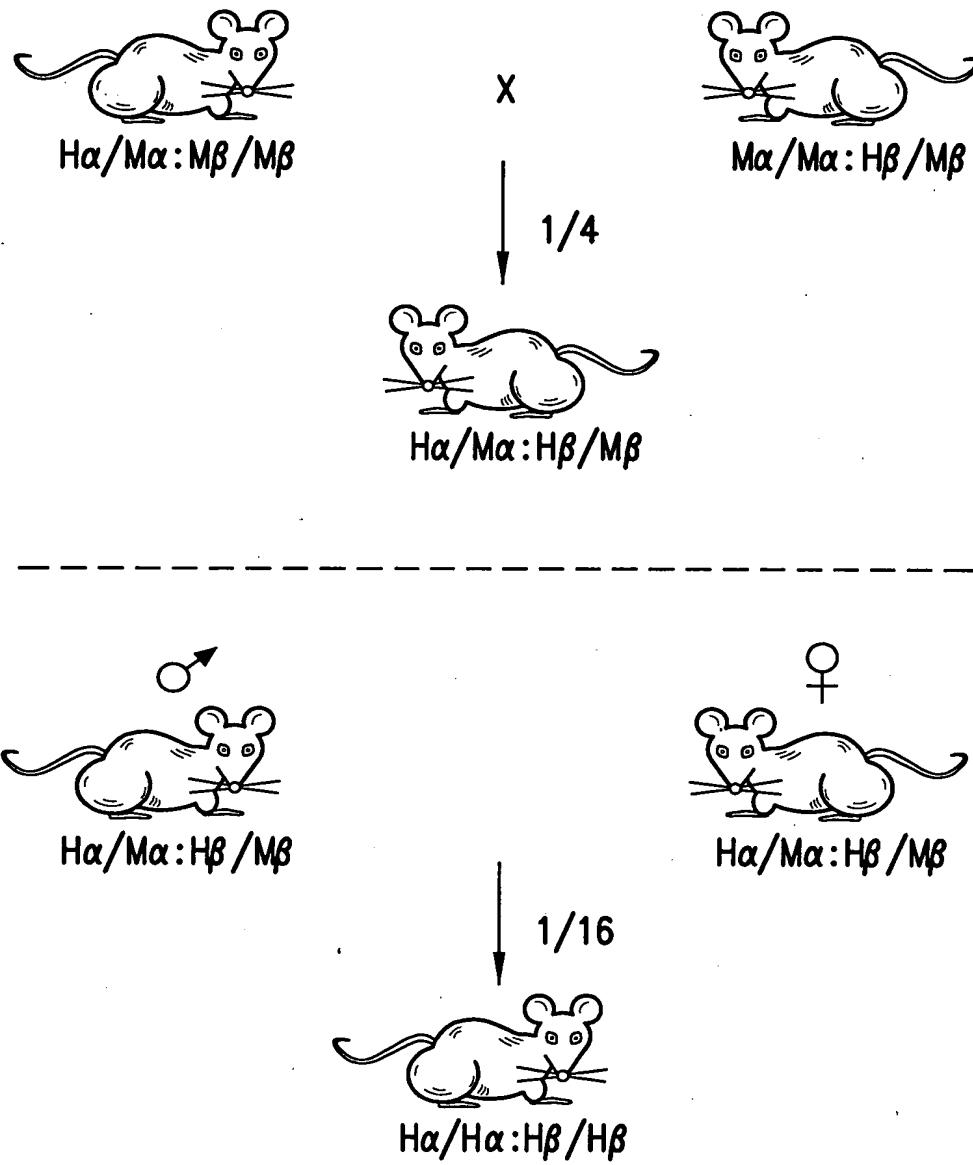


FIG. 1

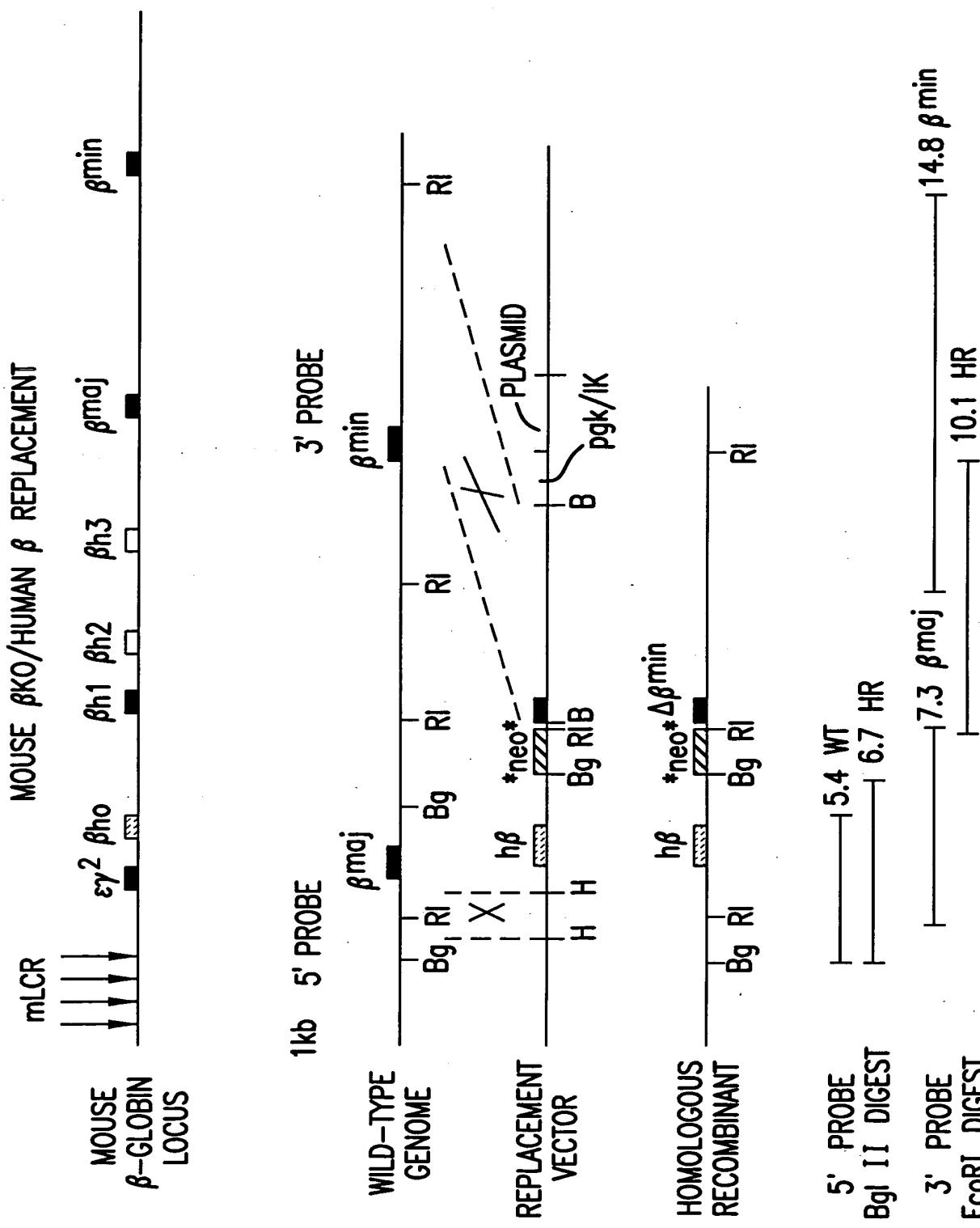
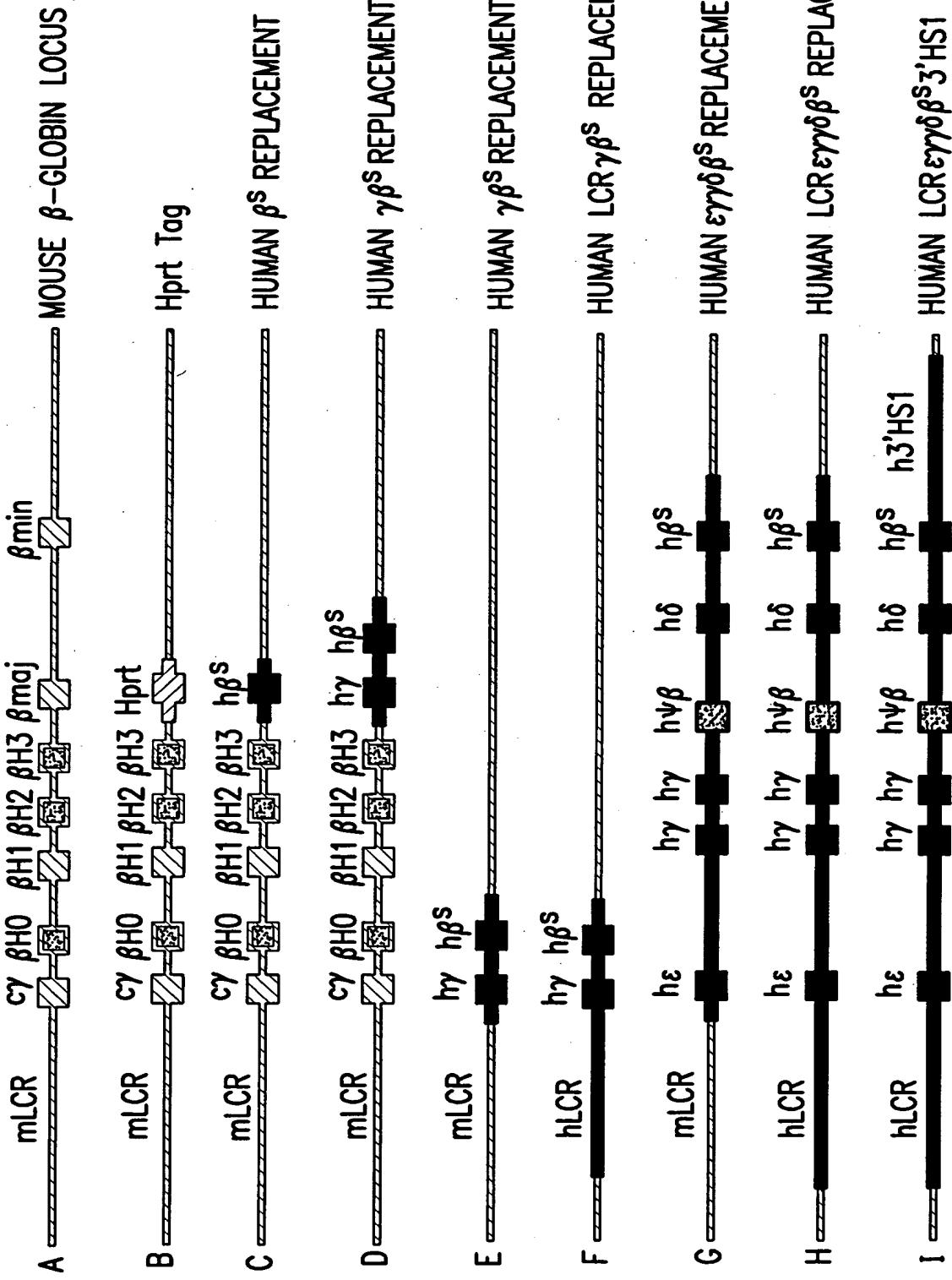


FIG. 2

## HUMAN REPLACEMENT OF THE MOUSE $\beta$ -GLOBIN LOCUS



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G  
E

HUMAN REPLACEMENT OF THE MOUSE  $\alpha$ -GLOBIN LOCUS

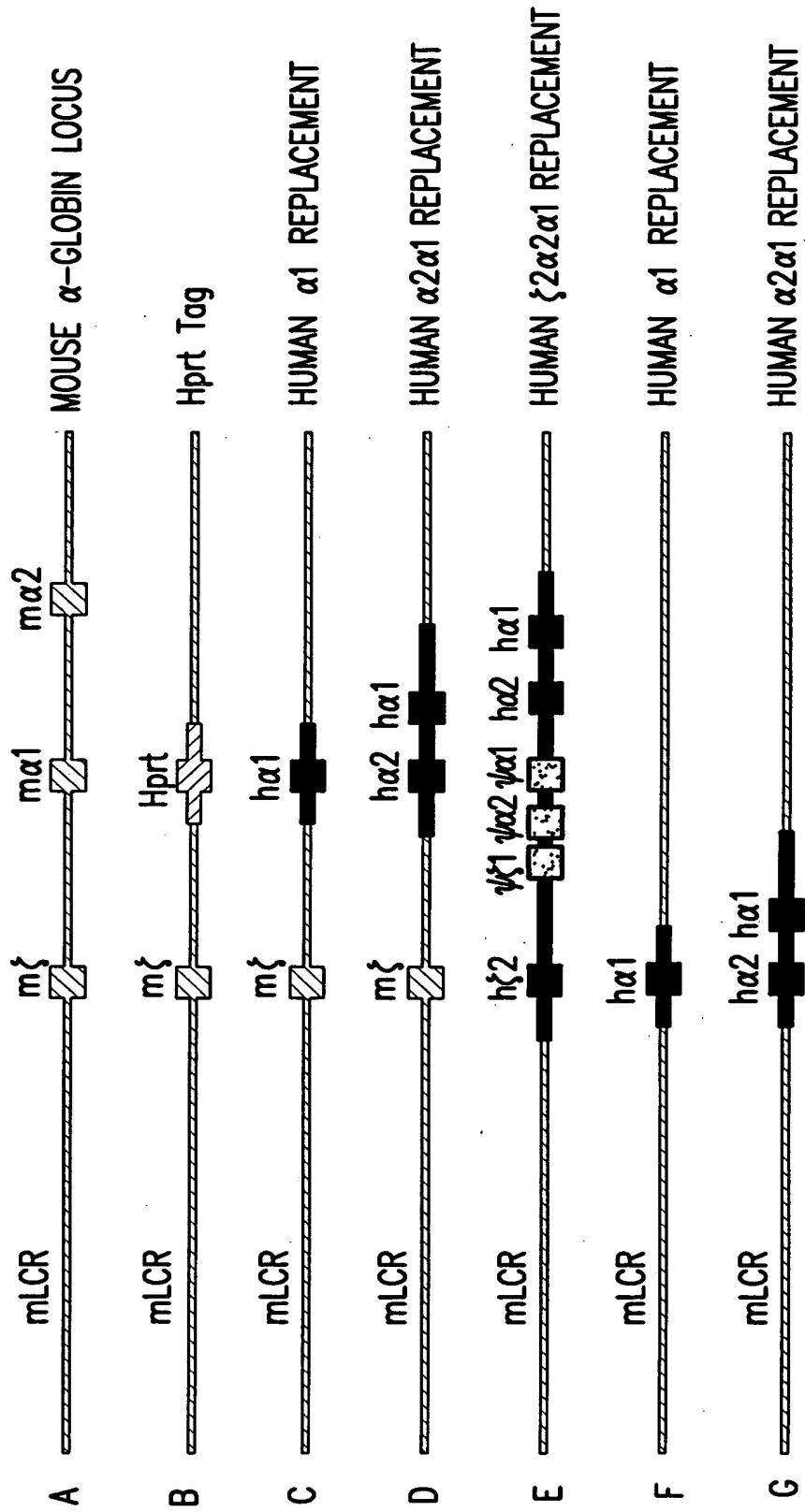


FIG. 4

PRODUCTION OF TRANSGENIC HbF → HbA MICE  
 (DOUBLY HOMOZYGOUS FOR MOUSE  $\alpha$ -GLOBIN AND  $\beta$ -GLOBIN DELETIONS)

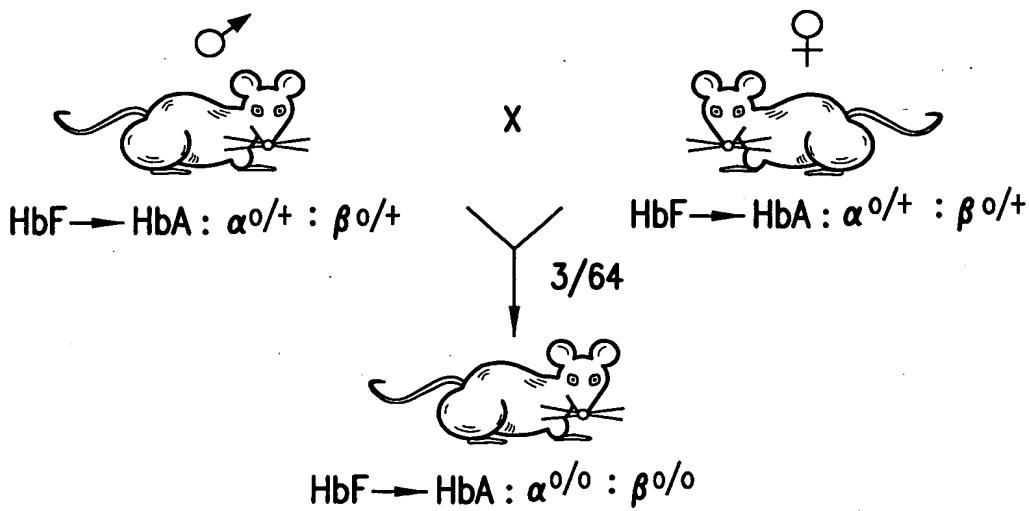
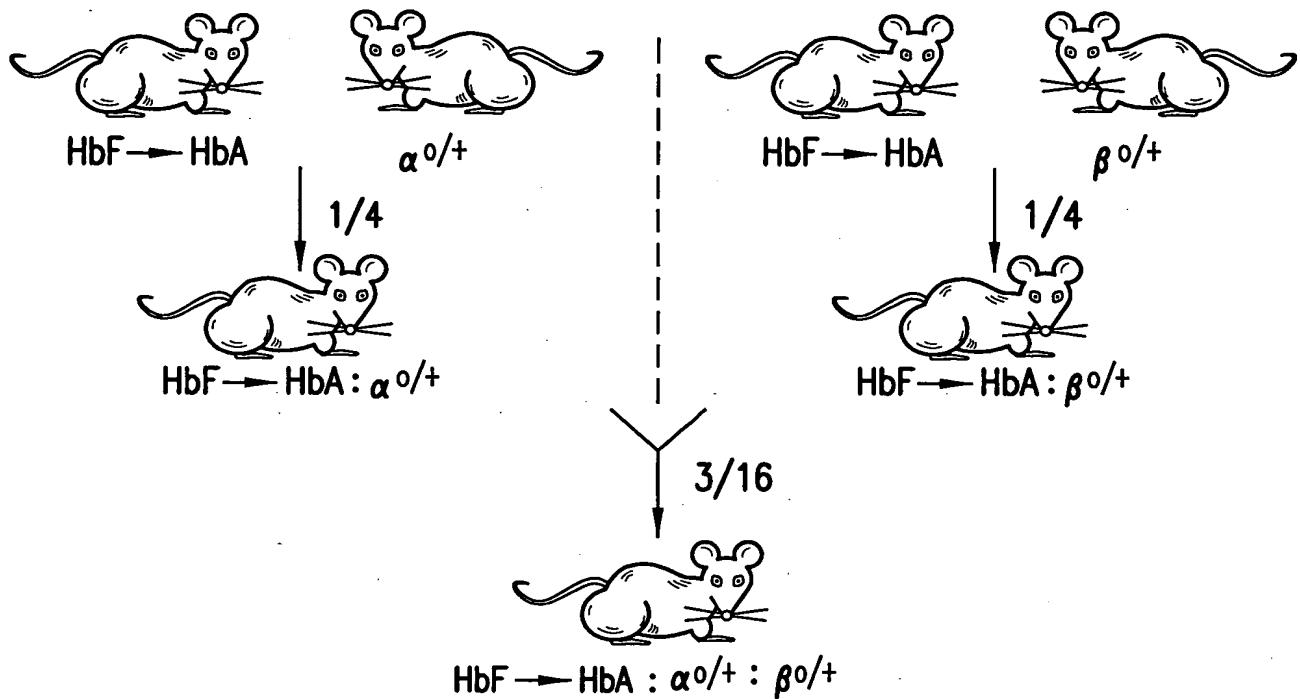
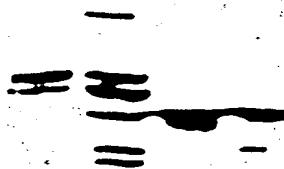


FIG.5

Isoelectric Focusing Gel Of  
Transgenic Mouse Hemolysates

1 2 3 4



1. Mouse Control
2. HbF → HbA :  $\alpha^{+/+}$  :  $\beta^{+/+}$  Mouse
3. HbF → HbA :  $\alpha^{0/0}$  :  $\beta^{0/0}$  Mouse
4. Human AA Control

**FIG.6**

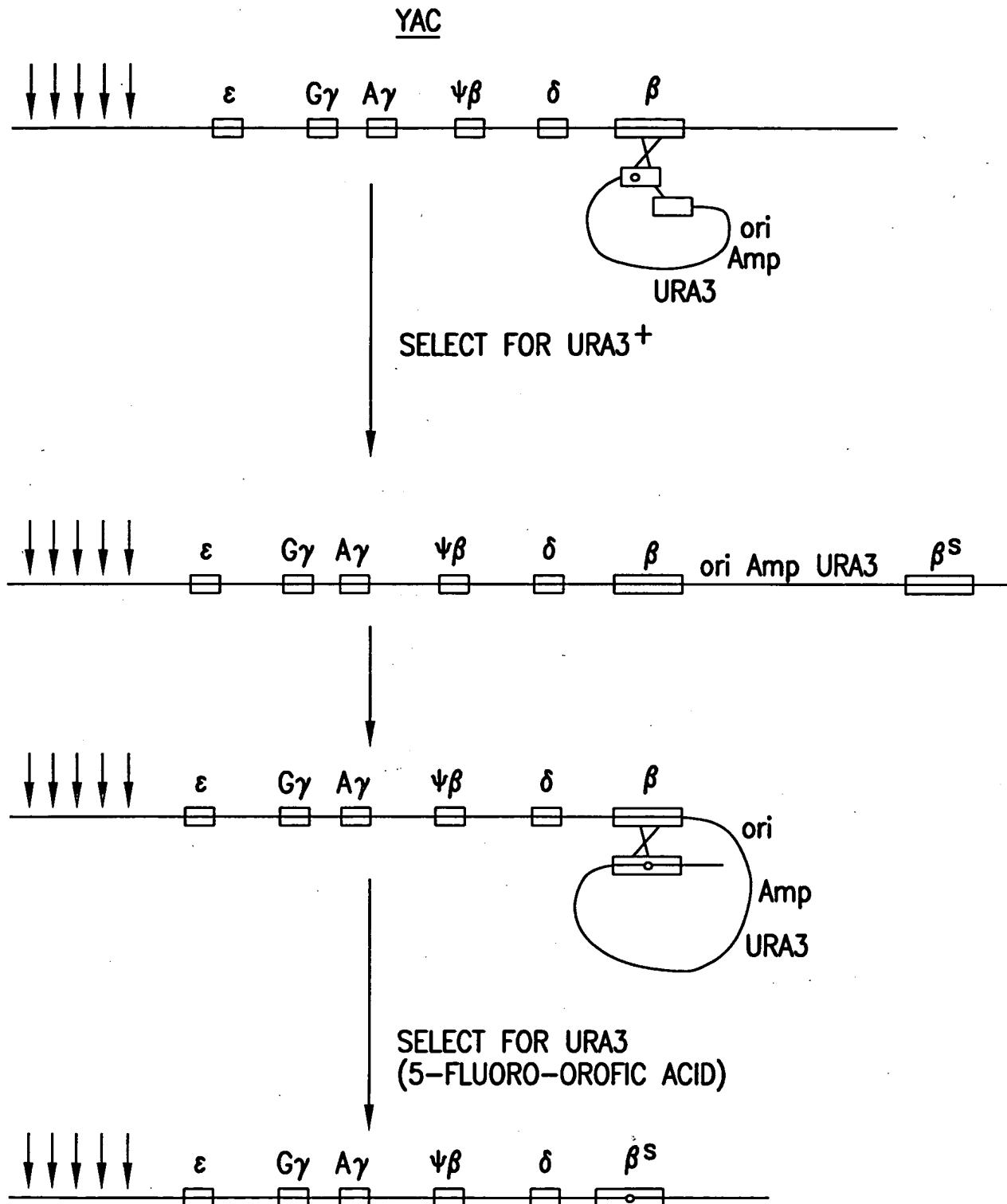


FIG. 7

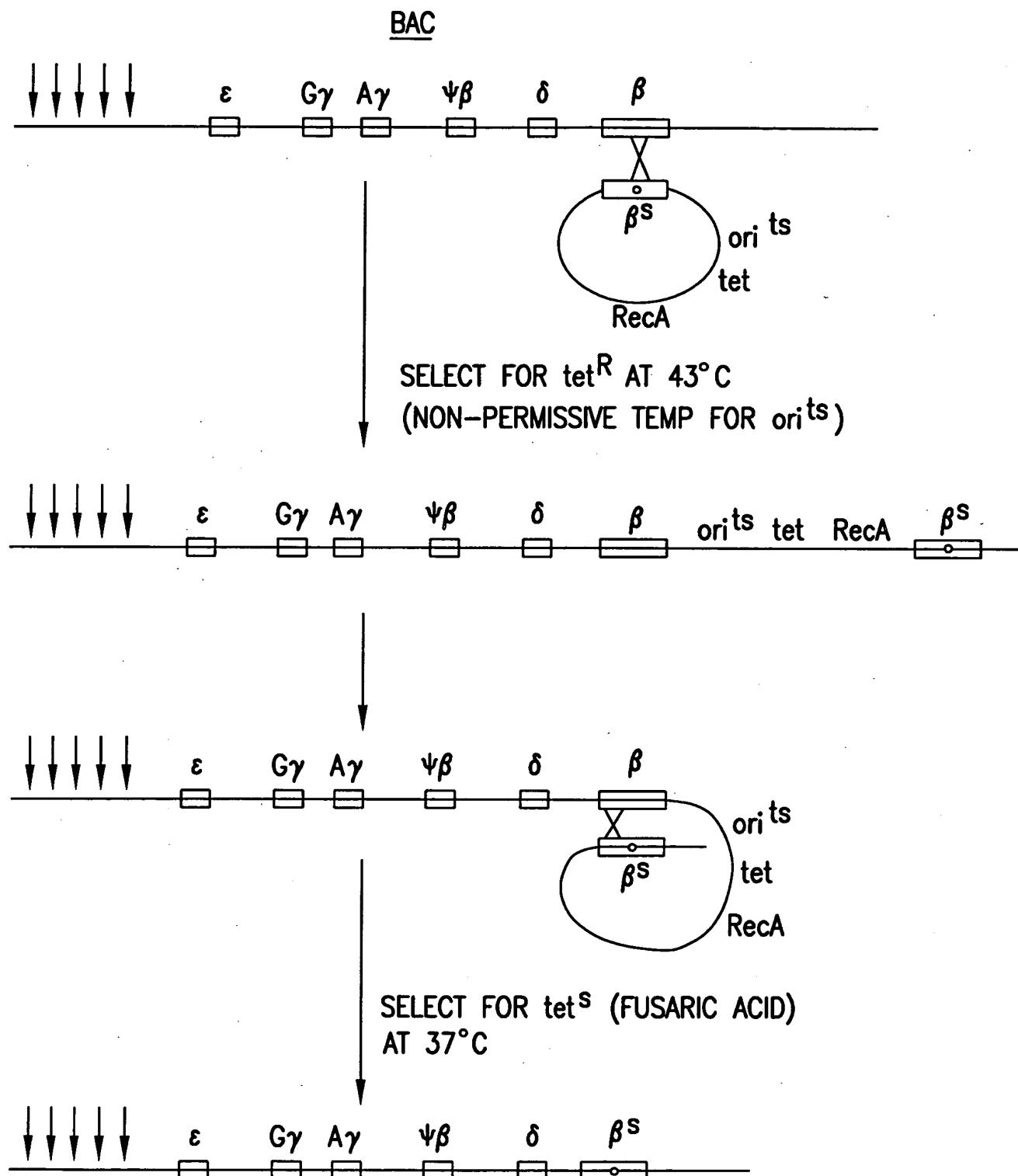
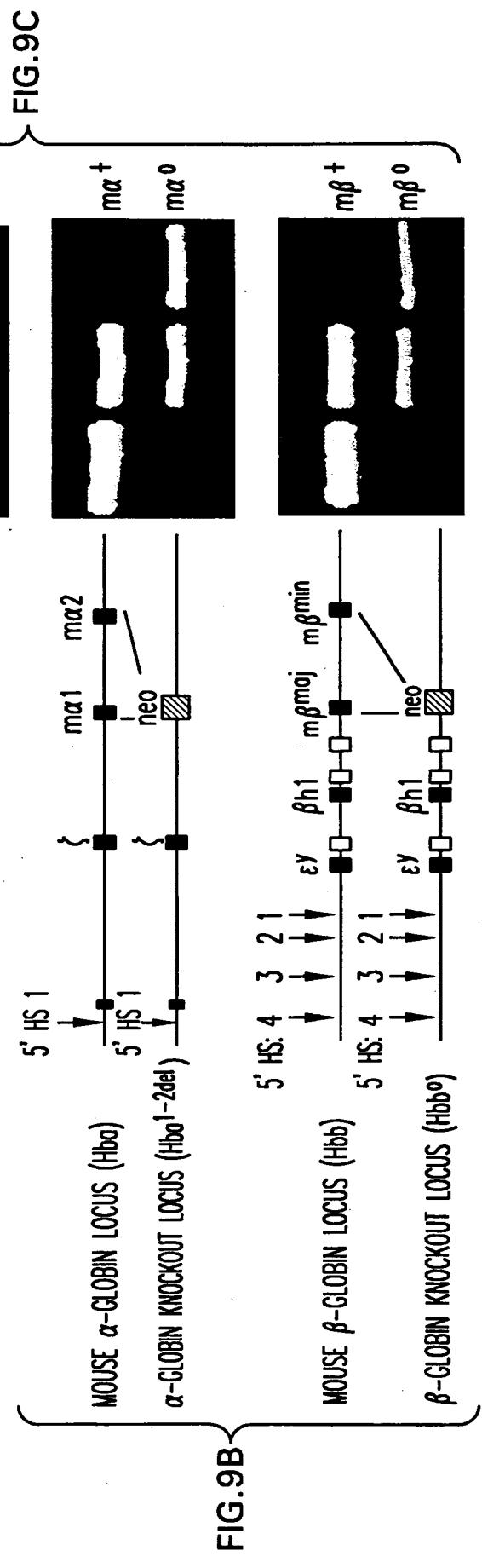
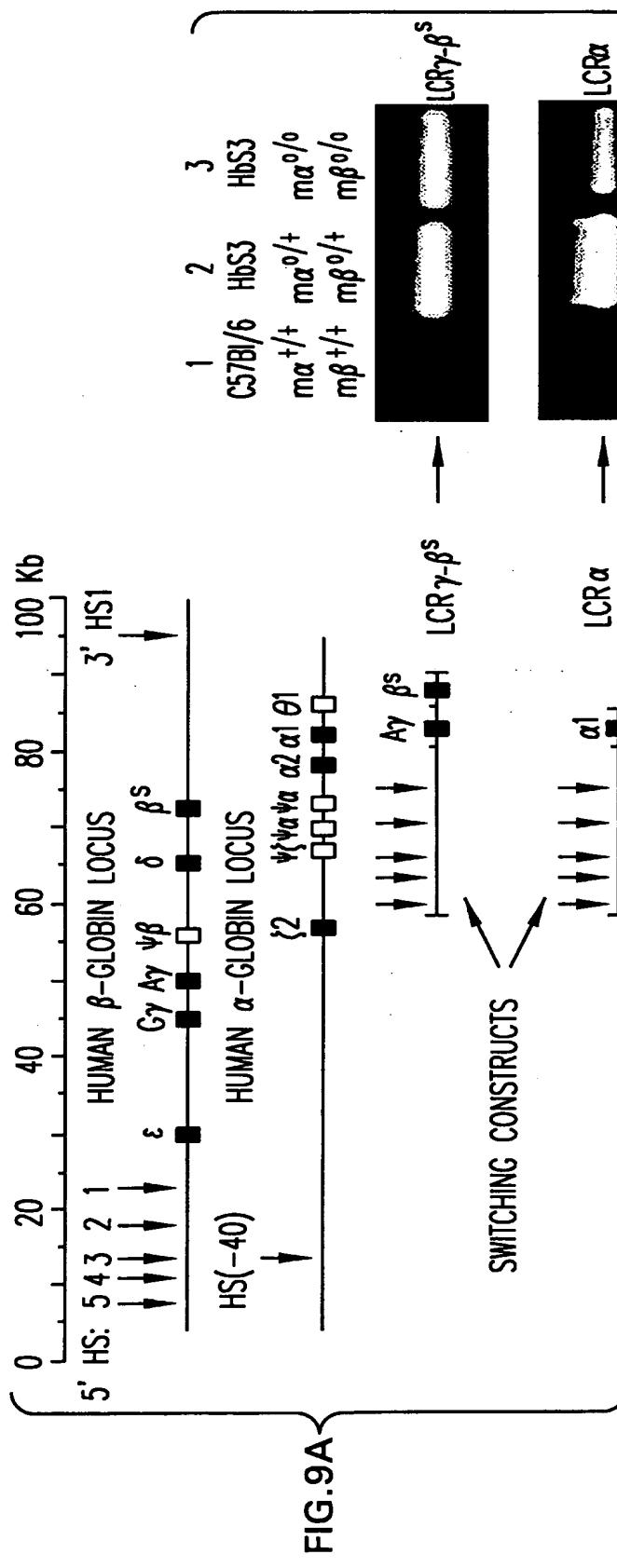


FIG.8



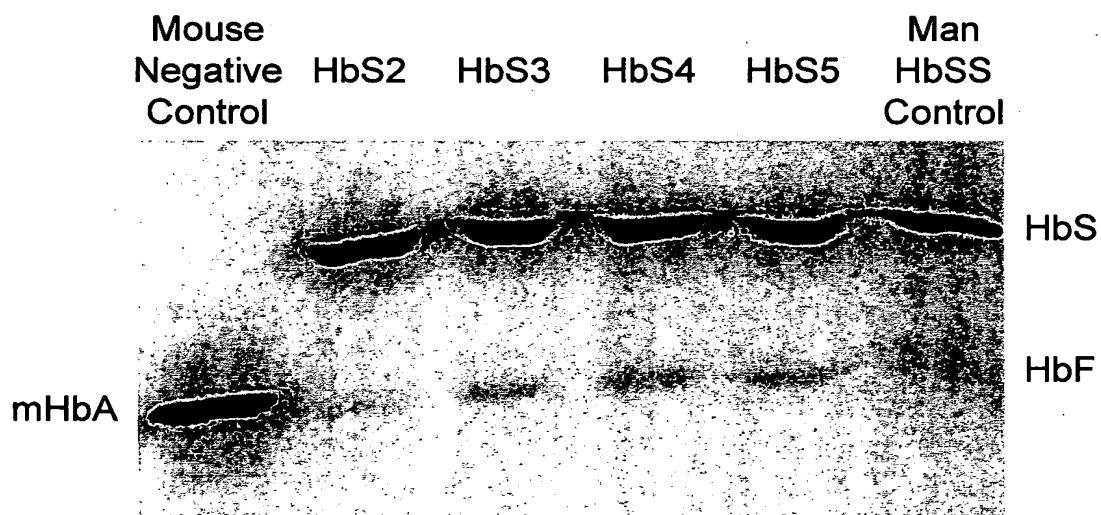


FIG. 10

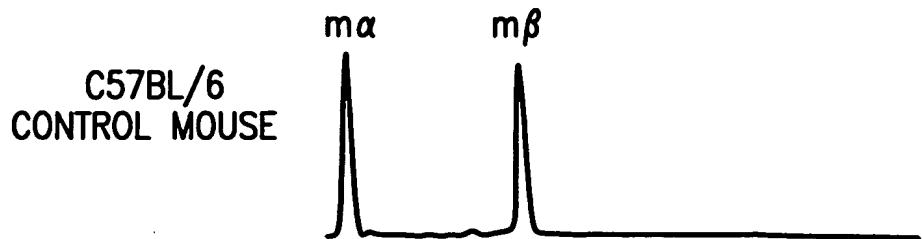


FIG. 11A

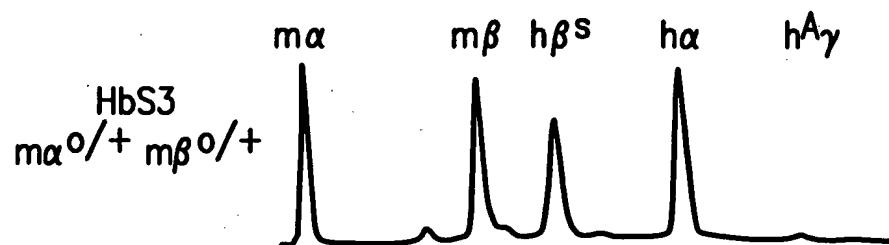


FIG. 11B

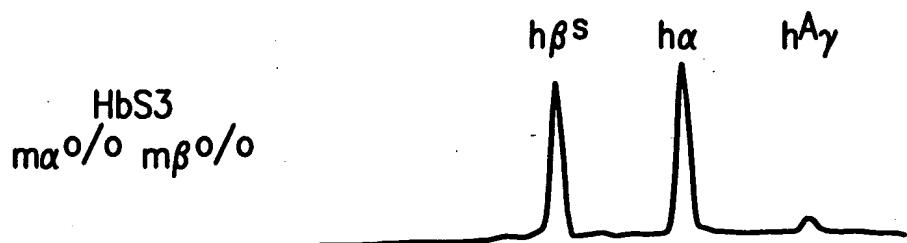


FIG. 11C

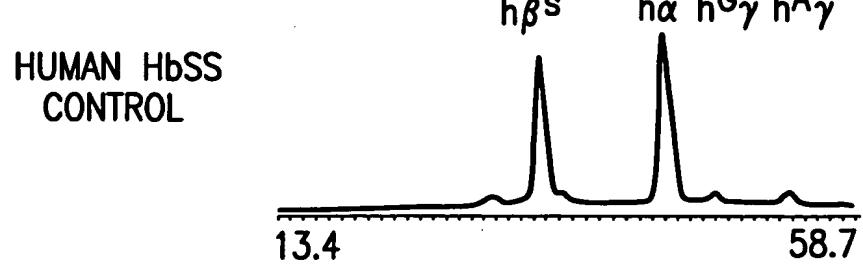


FIG. 11D

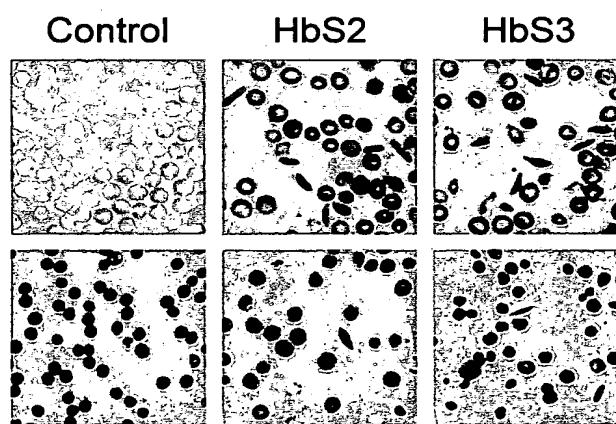


FIG. 12

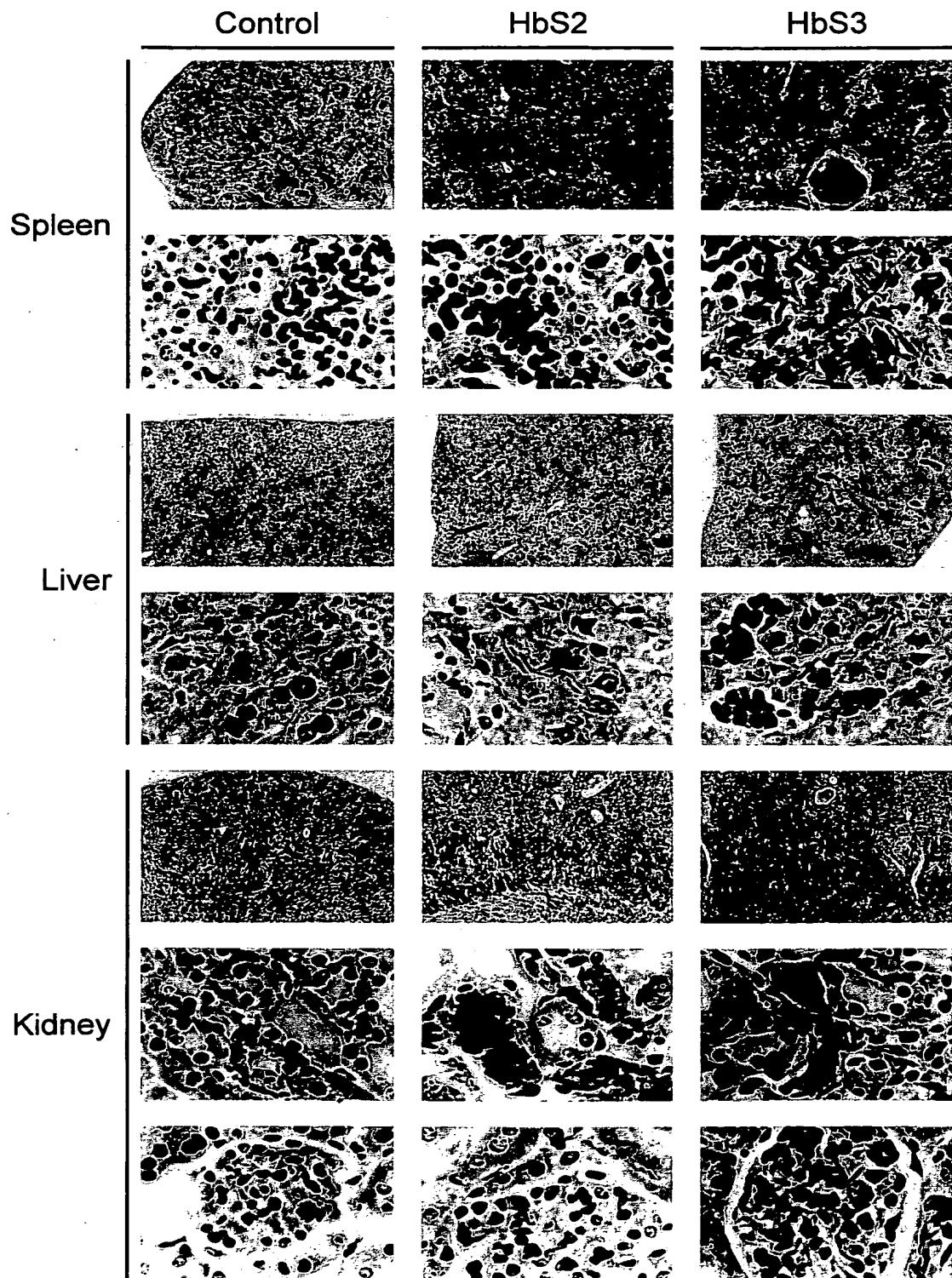


FIG. 13



**FIG. 14A**



**FIG. 14B**

### HEMOGLOBIN SWITCHING IN HbA MICE

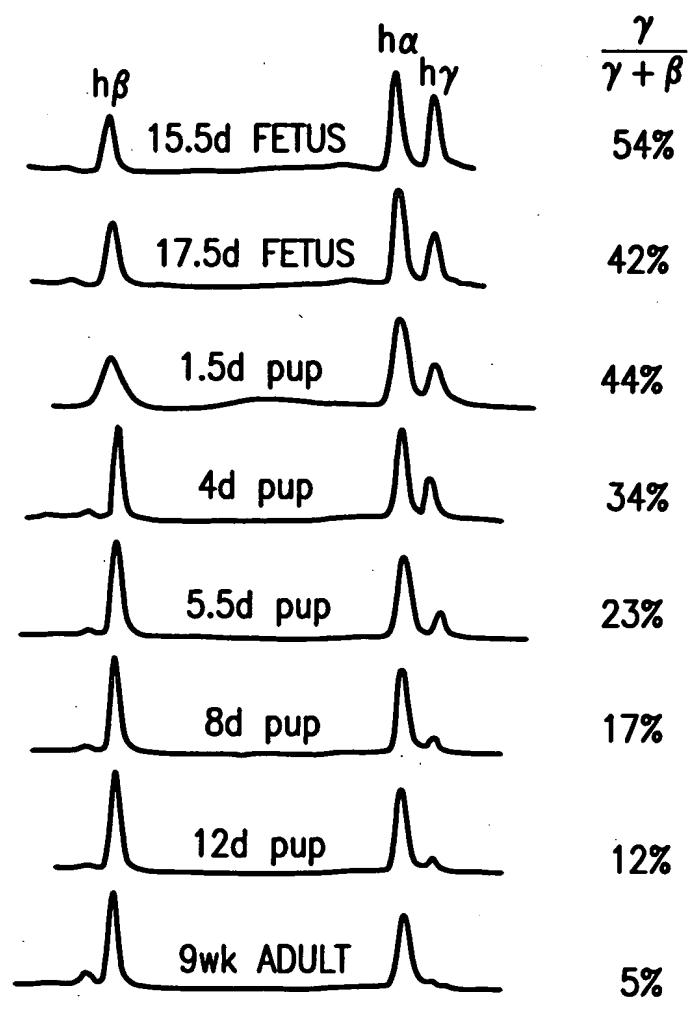


FIG. 15

## INCREASING HbF LEVELS IN HbS MICE: CROSSING THE HbS 3 AND HbF LINES

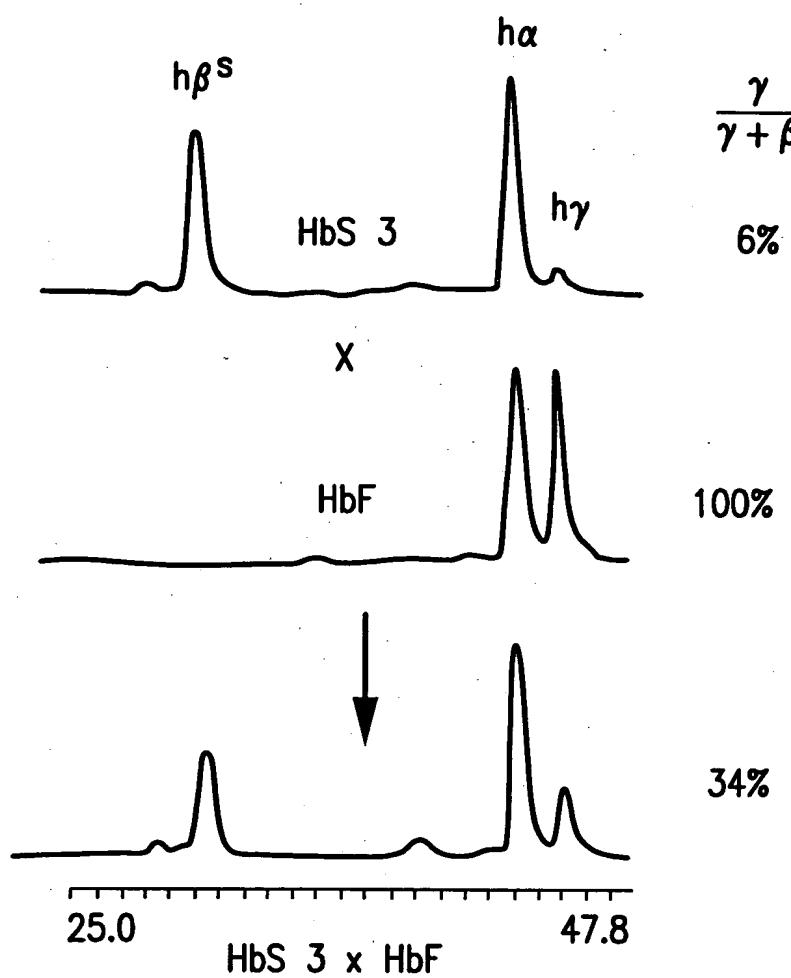


FIG. 16